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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,522	09/28/2001	Thomas Krahn	Bayer 10,139.3-KGB	5606
27384	7590	10/06/2006	EXAMINER	
NORRIS, MCLAUGHLIN & MARCUS, PA			DO, PENSEE T	
875 THIRD AVENUE			ART UNIT	
18TH FLOOR.			PAPER NUMBER	
NEW YORK, NY 10022			1641	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 09/966,522	Applicant(s) KRAHN ET AL.	
	Examiner Pensee T. Do	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 6-42 is/are pending in the application.
- 4a) Of the above claim(s) 6-16 and 24-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 6-42 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 25, 2006 has been entered.

### ***Amendment Entry & Claims Status***

All rejections in the previous office action are withdrawn because the prior arts fails to teach that the fluorescent dye permeates or able to pass through the pores or interstices of the cell membrane.

Claims 6-42 are pending.

Claims 17-23 are being examined.

Claims 6-16, 24-42 are withdrawn from further consideration.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

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one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The present specification fails to disclose or describe that the fluorescent dye and the masking dye are packaged in a kit. The specification fails to provide support for a kit comprising a fluorescent dye wherein said fluorescent dye is permeant to the membrane of a biological cell; and a masking dye wherein the masking dye is impermeant to the membrane of said biological cell. The present specification describes a method for masking the background fluorescence in quantitative fluorescence measurement in biomedical assays, connected with an increased in the sensitivity but fails to describe a kit comprising of a fluorescent dye and a masking dye.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 17-21, 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Wan et al. (Journal of Immunological Methods 162 (1993) pp. 1-7) in view of Cabbage et al. (US 5,582,982).

Wan teaches a method of using fluorescein conjugated E.Coli particles and second dye such as Trypan blue to quench the extracellular fluorescence in the solution. That means Trypan blue absorbs and the extracellular fluorescence which

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cause the solution to emit non-specific background light in the solution while the fluorescent that absorbs into the cells are being measured. Quenching the extracellular fluorescence thus means reducing non-specific background light in solution. (see abstract, page 3 "Phagocytosis assay" and "results"). Trypan blue is obviously impermeant to the membrane of the cell because it quenches extracellular fluorescence. If it is permeable to the membrane, then it would quench all the fluorescence that absorbs into the cells and there would be no fluorescence left to detect. Wan also teaches that the concentration of trypan blue require to completely quench extracellular fluorescence was determined by exposing  $3$  or  $6 \times 10^8$  particles/well to serial dilutions of the dye in a 96-well plate. Complete quenching of the fluorescence was obtained with 250 ug/ml of the dye. Thus, Wan meets the requirement that the non-specific background in solution is reduced by at least 30%, 50% and 70% (claims 18-20). Since Wan teaches a fluorescent dye attached to the cell as in the present invention, such fluorescent dye is inherently permeant to the membrane of the cell and detects a voltage across the membrane of the cell. Since trypan blue can quench or reduce non-specific background, it would inherently be able to perform functions such as to improve the signal to noise ratio by at least 300%.

However, Wan fails to teach these reagents packaged in a kit.

Cubbage teaches a kit comprising a fluorescent probe and a background-reducing compound that diffuses into and onto the biological entity. (see col. 2, line 45-col. 7, line 27).

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It would have been obvious to one of ordinary skills in the art package the components taught by Wan into a kit as taught by Cubbage for cost effective or other economic advantages.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wan et al. (Journal of Immunological Methods 162 (1993) pp. 1-7) in view of Cubbage et al. (US 5,582,982) as applied to claim 17-21, 23 above, and further in view of Van Aken (US 5,489,537).

Wan and Cubbage have been discussed above.

However, Wan and Cubbage fails to teach Brilliant Black as a fluorescent dye.

Van Aken teaches a method and kit for determining the presence or absence of a substance by detection of a colloidal dye associated with agglutinated particles. The colloidal dye is a background-enhancing dye, which reduces non-specific background to enhance optical detection. The background-enhancing dye is a water-soluble dye such as Brilliant Black. (see col. 21, lines 58-67).

It would have been obvious to one of ordinary skills in the art to use Brilliant Black as a masking or quenching dye in the kit for use in the method of Wan and Cubbage because both references teach using quenching or background reducing dye, which reduces background light in assay. Since Brilliant Black is known for enhancing the background in an assay, which uses optical detection, it would motivate one of ordinary skills in the art to use Brilliant Black in assays such as one taught by Wan and Cubbage because both Wan and Cubbage teach using fluorescent label, which is known for producing non-specific background.

### ***Response to Arguments***

Applicant's arguments filed August 25, 2006 have been fully considered but they are not persuasive.

Applicants argue that the fluorescent dye in Wan does not permeate the cell membrane and defined "permeate" as to "pass through the pores or interstices of". The fluorescent dye in Wan is conjugated to E. coli particles that have been phagocytised, i.e. taken up, internalized, by Wan's cell.

Since the fluorescent dye of the present invention and the fluorescent dye of Wan are the same, it is inherent that Wan's fluorescent dye can permeate the cell membrane in the same way as that of the present invention.

### ***Conclusion***


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Pensee T. Do  
Patent Examiner  
September 25, 2006

  
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